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Table 13. Characteristics of Protease Inhibitors (PIs)

Generic Name/ Trade Name	Formulation	Dosing Recommendations	Food Effect	Oral Bio- availability	Serum half-life	Route of Metabolism	Storage	Adverse Events
Amprenavir (APV)/ Agenerase®	50 mg capsules, 15 mg/mL oral solution (capsules and solution NOT inter-changeable on mg per mg basis) Note: APV 150 mg capsule is no longer available; consider using fosamprenavir in these patients.	1400 mg two times/day (oral solution) Note: APV and RTV oral solution should not be co-administered because of competition of the metabolic pathway of the two vehicles.	High-fat meal decreases blood concentration 21%; can be taken with or without food, but high fat meal should be avoided.	Not determined in humans	7.1–10.6 hours	Cytochrome P450 3A4 inhibitor, inducer, and substrate Dosage adjustment in hepatic insufficiency recommended (See Table 14)	Room temperature (up to 25°C or 77°F)	<ul style="list-style-type: none"> • GI intolerance, nausea, vomiting, diarrhea • Rash • Oral paresthesias • Hyperlipidemia • Transaminase elevation • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia Note: Oral solution contains propylene glycol; contraindicated in pregnant women, children <4 years old, patients with hepatic or renal failure, & patients treated with disulfiram or metronidazole
Atazanavir (ATV)/ Reyataz™	100, 150, 200 mg capsules	400 mg once daily <u>If taken with efavirenz or tenofovir:</u> RTV 100 mg + ATV 300 mg once daily	Administration with food increases bioavailability Take with food; avoid taking with antacids	Not determined	7 hours	Cytochrome P450 3A4 inhibitor and substrate Dosage adjustment in hepatic insufficiency recommended (See Table 14)	Room temperature (up to 25°C or 77°F)	<ul style="list-style-type: none"> • Indirect hyperbilirubinemia • Prolonged PR interval – some patients experienced asymptomatic 1st degree AV block • Use with caution in patients with underlying conduction defects or on concomitant medications that can cause PR prolongation • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia
Fosamprenavir (f-APV)/ Lexiva™	700 mg tablet	<u>ARV-naïve patients:</u> <ul style="list-style-type: none"> • f-APV 1,400 mg two times/day; or • (f-APV 1,400 + RTV 200 mg) once daily; or • (f-APV 700 mg + RTV 100mg) two times/day <u>PI-experienced pts (once daily regimen not recommended):</u> <ul style="list-style-type: none"> • (f-APV 700mg + RTV 100mg) two times/day <u>Co-administration w/ EFV (Unboosted f-APV not recommended):</u> <ul style="list-style-type: none"> • (f-APV 700 mg + RTV 100mg) two times/day; or • (f-APV 1,400 mg + RTV 300 mg) once daily 	No significant change in amprenavir pharmacokinetics in fed or fasting state	Not established	7.7 hours (amprenavir)	Amprenavir is a cytochrome P450 3A4 inhibitor, inducer, and substrate Dosage adjustment in hepatic insufficiency recommended (See Table 14)	Room temperature (up to 25°C or 77°F)	<ul style="list-style-type: none"> • Skin rash (19%) • Diarrhea, nausea, vomiting • Headache • Hyperlipidemia • Transaminase elevation • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia
Indinavir/ Crixivan®	200, 333, 400 mg capsules	800 mg every 8 hours; <u>With RTV:</u> [IDV 800 mg + RTV 100 or 200 mg] every 12 hours	<u>For unboosted IDV</u> Levels decrease by 77% Take 1 hour before or 2 hours after meals; may take with skim milk or low-fat meal <u>For RTV-boosted IDV:</u> Take with or without food	65%	1.5–2 hours	Cytochrome P450 3A4 inhibitor (less than ritonavir) Dosage adjustment in hepatic insufficiency recommended (See Table 14)	Room temperature 15–30°C (59–86°F), protect from moisture	<ul style="list-style-type: none"> • Nephrolithiasis • GI intolerance, nausea • Indirect hyperbilirubinemia • Hyperlipidemia • Misc.: Headache, asthenia, blurred vision, dizziness, rash, metallic taste, thrombocytopenia, alopecia, and hemolytic anemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia

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Lopinavir + Ritonavir (LPV/r)/ Kaletra®	Each tablet contains LPV 200 mg + RTV 50 mg Oral solution: Each 5 mL contains LPV 400 mg + RTV 100 mg Note: Oral solution contains 42% alcohol	LPV 400 mg + RTV 100 mg (2 tablets or 5 mL) twice daily or LPV 800mg + RTV 200mg (4 tablets or 10mL) once daily (Note: once-daily dosing only recommended for treatment-naïve pts; not for patients receiving EFV, NVP, f-APV, or NFV) <u>With EFV or NVP:</u> <u>For treatment-experienced pts:</u> LPV 600 mg + RTV 150 mg (3 oral tablets) twice daily or LPV 533 mg + RTV 133 mg (6.7 mL oral solution) twice daily with food	Oral tablet - No food effect; take with or without food Oral solution - Moderately fatty meal ↑ LPV AUC & Cmin by 80% & 54%, respectively; take with food	Not determined in humans	5–6 hours	Cytochrome P450 (3A4 inhibitor and substrate)	Oral tablet is stable at room temperature Oral solution is stable at 2°–8°C until date on label; is stable when stored at room temperature (up to 25°C or 77°F) for 2 months	<ul style="list-style-type: none"> • GI intolerance, nausea, vomiting, diarrhea (higher incidence with once-daily than twice-daily dosing) • Asthenia • Hyperlipidemia (esp. hypertriglyceridemia) • Elevated serum transaminases • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia
Nelfinavir (NFV)/ Viracept®	250 mg tablets or 625 mg tablets 50 mg/g oral powder	1,250 mg two times/day or 750 mg three times/day	Levels increase 2–3 fold Take with meal or snack	20–80%	3.5–5 hours	Cytochrome P450 3A4 inhibitor and substrate	Room temperature 15–30°C (59–86°F)	<ul style="list-style-type: none"> • Diarrhea • Hyperlipidemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes among patients with hemophilia • Serum transaminase elevation
Ritonavir (RTV)/ Norvir®	100 mg capsules or 600 mg/7.5 mL solution	600 mg every 12 hours (when ritonavir is used as sole PI) As pharmacokinetic booster for other PIs – 100 mg – 400 mg per day – in 1–2 divided doses	Levels increase 15% Take with food if possible; this may improve tolerability	Not determined	3–5 hours	Cytochrome P450 (3A4 > 2D6; Potent 3A4 inhibitor)	Refrigerate capsules Capsules can be left at room temperature (up to 25°C or 77°F) for ≤30 days; Oral solution should NOT be refrigerated	<ul style="list-style-type: none"> • GI intolerance, nausea, vomiting, diarrhea • Paresthesias – circumoral and extremities • Hyperlipidemia, esp. hypertriglyceridemia • Hepatitis • Asthenia • Taste perversion • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia
Saquinavir tablets and hard gel capsules (SQV)/ Invirase®	200 mg capsules, 500 mg tablets	Unboosted SQV not recommended <u>With RTV:</u> <ul style="list-style-type: none"> • (RTV 100 mg + SQV 1,000 mg) two times/day 	Take within 2 hours of a meal when taken with RTV	4% erratic (when taken as sole PI)	1–2 hours	Cytochrome P450 (3A4 inhibitor and substrate)	Room temperature 15–30°C (59–86°F)	<ul style="list-style-type: none"> • GI intolerance, nausea and diarrhea • Headache • Elevated transaminase enzymes • Hyperlipidemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia

* Dose escalation for Ritonavir when used as sole PI: Days 1 and 2: 300 mg two times; day 3–5: 400 mg two times; day 6–13: 500 mg two times; day 14: 600 mg two times/day.

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Saquinavir soft gel capsule (SQV-sgc)/ Fortovase®	200 mg capsules Anticipated discontinuation of distribution in 2006	Unboosted SQV-sgc: 1,200 mg three times/day <u>With RTV:</u> <ul style="list-style-type: none"> (RTV 100 mg + SQV-sgc 1,000 mg) two times/day 	Levels increase 6-fold. Take with or up to 2 hrs after a meal – as sole PI or with RTV	Not determined	1–2 hours	Cytochrome P450 (3A4 inhibitor (less than ritonavir)	Refrigerate or store at room temperature ($\leq 25^{\circ}\text{C}$ or 77°F) for up to 3 months)	<ul style="list-style-type: none"> GI intolerance, nausea, diarrhea, abdominal pain and dyspepsia Headache Hyperlipidemia Elevated transaminase enzymes Hyperglycemia Fat maldistribution Possible increased bleeding episodes in patients with hemophilia
Tipranavir (TPV)/ Aptivus®	250 mg capsules	500 mg twice daily with ritonavir 200 mg twice daily Unboosted tipranavir is <u>not</u> recommended	Take both TPV & RTV with food. Bio-availability increased with high fat meal	Not determined	6 hours after single dose of TPV/ RTV	TPV – Cytochrome P450 (3A4 inducer and substrate) Net effect when combined with RTV – CYP 3A4 inhibitor and CYP 2D6 inhibitor	Refrigerated capsules are stable until date on label; if stored at room temperature (up to 25°C or 77°F) – must be used within 60 days	<ul style="list-style-type: none"> Hepatotoxicity – clinical hepatitis including hepatic decompensation has been reported, monitor closely, esp. in patients with underlying liver diseases Skin rash – TPV has a sulfonamide moiety, use with caution in patients with known sulfonamide allergy Hyperlipidemia (esp. hypertriglyceridemia) Hyperglycemia Fat maldistribution Possible increased bleeding episodes in patients with hemophilia

* Dose escalation for ritonavir when used as sole PI: Days 1 and 2: 300 mg two times; day 3-5: 400 mg two times; day 6-13: 500 mg two times; day 14: 600 mg two times/day.